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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/462,682	04/28/2000	DAVID J. FITZGERALD	015280-31010	5396

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/462,682	FITZGERALD, DAVID J.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,11-23,26,28,31,32,34-36,39-43,46-50* is/are pending in the application.

4a) Of the above claim(s) *4-6,11,14-23,26,28,31,32,34-36 and 39-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7,8,12,13 and 46-50* is/are rejected.

7)☒ Claim(s) *2,7 and 8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/23/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3, 7-8, 12-13, and 46-50 are under consideration. Claims 1-2, and 12 have been amended. All other claims have either been withdrawn from consideration or canceled.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections Withdrawn

2. Claim 1 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, has been obviated through amendment of claim 1 to recite a SEQ ID NO, and the newly submitted combination of claim limitations necessitating a different grounds of rejection/objection under 35 USC 112, first paragraph set forth below.

3. Claim 1 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, in light of the responses and amendment of claim 1 addressing the issues made of record.

4. Claims 1,3,7-8,12-13 rejected under 35 U.S.C. 102(e) as being anticipated by Murphy has been obviated through amending claim 1 to define the immunogen to lack ADP ribosylating activity, and the immunogen of Murphy evidences ADP ribosylating activity.

5. Claims 1,7-8,12-12 rejected under 35 U.S.C. 102(e) as being anticipated by Pastan et al (6,074,644 and 6,011,002) have been obviated through Applicant's traversal that the epitope inserted in the loop must be an epitope from a pathogenic organism, and not just any enzyme or other biological molecule.

Rejection Maintained

6. Claims 1-3, 7-8, 12-13, and new claims 46-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wels et al (6,498,233) in view of Pastan et al (6,074,644) is maintained for reasons of record, and the fact that the nucleic acid binding domain of Wels is disclosed to be obtained from yeast, and to include GAL4 amino acids 1 to 147 (see Wels et al, brief summary test, paragraph 32) .

Response to Arguments

* The rejection of claims 1-3, 7-8, 12-13, 46-50 under 35 U.S.C. 103(a) as being unpatentable over Wels et al (6,498,233) in view of Pastan et al (6,074,644) is traversed on the grounds that the "nucleic acid binding domain of Wels is not a nucleic acid binding protein".

7. The examiner would like to direct Applicant to column 7, lines 60-67 and column 8, lines 1-34 of Wels et al ('233), where the reference defines the nucleic acid binding domain to be a GAL4 amino acid sequence of amino acids 1-47 and is obtainable from yeast; yeast being an organism known to be pathogenic.

8. Therefore, contrary to Applicant's assertion that the inserted nucleic acid binding domain is not a protein, the molecule is a protein sequence of amino acids (GAL4), which does bind to a nucleic acid sequence, is taught to be obtainable from yeast, a type of pathogen known to cause disease. Therefore the combination of Wels et al in view of Pastan et al does satisfy all of the elements of the claims, in view of the nucleic acid binding domain having been defined to be about 148 amino acids in length (see col. 8, lines 1-34).

Information Disclosure Statement

9. The information disclosure statement filed February 23,2004 has been considered.

New Claims Limitations/New Grounds of Rejection

Claim Objections

10. Claims 2, 7 and 8 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

11. Claim 2 depends from amended claim 1 and defines the translocation domain to be domain II of PE, while claim 1 defines the translocation domain to be a range of amino acids

from SEQ ID NO 2, specifically amino acids 280-344. Claim 1 also recites that that translocation domain can be larger, smaller or differ from amino acids 280-344 of SEQ ID NO 2, as long as the domain sequence shares 90% sequence identity with amino acids 280-344 of SEQ ID NO 2. The translocation domain II of claim 1 may be of any length from 58 amino acids to 72 amino acids based upon the recitation of the phrase 90% identical to the sequence of amino acids 280-344 of SEQ ID NO 2. The translocation domain II of PE, contains 84 amino acids. Claim 2 is not further limiting of claim 1 from which it depends because through the broad recitation of domain II, claim 2 sets forth a species which claim 1 does not provide support in light of the amendment of claim 1 to recite a specific range of amino acids for domain II. The complete domain II of PE lacks support in claim 1 which requires domain II to be limited to a fragment of domain II through the recitation of a portion of the PE domain II of 65 amino acids in length, and may be larger or smaller than the recited range of 65 amino acids, but the resultant molecule must share 90% identity with the recited range. The upper limit in size would therefore be 72 amino acids, a molecule that is 110% of the recited range of amino acids, the range defining 100% of the domain II fragment, and the claim permits an additional 10% variation in size, through the recitation of 90% identical.

12. Claim 2 also defines the ER retention domain to be domain III of PE. Domain III of PE naturally evidencing ADP ribosylating activity. While claim 1 recites that the ER retention domain lacks ADP ribosylating activity, without reference to any specific molecule, sequence or structure. The recitation of domain III of PE, a specific molecule that has not been modified from the native sequence, sets forth a species of invention that broadens the scope of claim 1, by reciting claim limitations that encompass a domain that evidences ADP ribosylating activity.

13. Claim 2 broadens the scope of claim 1 from which it depends for the reasons set forth immediately above.

14. Claim 7 defines the translocation domain to comprise amino acids 280 to 364 of SEQ ID NO 2. Based upon the newly submitted combination of claim limitations set forth in claim 1, claim 7 is no longer further limiting of claim 1, by broadening the scope to include molecules that share less identity than 90% with the recited range of amino acids 280-344 of SEQ ID No 2, by defining the molecule of claim 7 to be 85 amino acids in length and the domain of claim 1 has an upper limit size of 72 amino acids. Claim 7 is not further limiting of claim 1 from which it depends, as claim 7 broadens the scope of newly amended claim 1.

15. Claim 8 defines the translocation domain II to be the translocation domain of PE. The translocation domain of claim 1 may be of any length from 58 amino acids to 72 amino acids based upon the recitation of the phrase 90% identical to the sequence of amino acids 280-344 of SEQ ID NO 2. The translocation domain II of PE, contains 84 amino acids. Claim 8 is not further limiting of claim 1 from which it depends because through the broad recitation of domain II, claim 8 sets forth a species which claim 1 does not provide support in light of the amendment of claim 1 to recite a specific range of amino acids for domain II. The complete domain II of PE lacks support in claim 1 which requires domain II to be limited to a fragment of domain II, and claim 8 also is not further limiting of claim 1 through reciting a molecule that shares less than 90% identity with the recited range of amino acids of claim 1.

Claim Rejections - 35 USC § 112

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Amended claim 1 and new claims 46 and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

Claim 1 and new claims 46 and 47 recite the phrase "comprising an amino acid sequence at least" 90% , 95% or 98% identical to the sequence of Pseudomonas aeruginosa (PE) (SEQ ID NO:2) from amino acid position 290 to amino acid 344. While figure 7 shows domain II to be defined by a stretch of amino acids from position 253 to 364, amino acids 253 to 279 and 345 to 364 not being essential and amino acids 280 to 344 as being essential, the instant specification does not disclose a genus of variants of the recited range of amino acids , specifically from position 280 to amino acid position 344, and shares 90% identity over this range of amino acids. The specification does not describe where or how the amino acids can be changed to preserve the biological activity of translocation.

The specification broadly describes as part of the invention translocation domains of PE, and suggests the utilization of molecules with differences in amino acid sequence at [0072] of the instant specification. The instant specification also suggests screening for molecules with a recited functionality based upon the required domain function, but the instant specification does not describe a genus of variant domain II molecules, that share only 90% identity over the range of amino acids from amino acid 280 to amino acid 344. A single species that shares 100% sequence identity with the amino acids sequence of SEQ ID NO 2, does not provide original descriptive support for a genus of molecules that may have deletions, insertions, substitutions or additions over the full length of the recited amino acid domain. None of these sequences meets

the written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

Applicants have described the region of amino acids from amino acid 280 to 344 as being critical to translocation domain activity for PE, but no amino acid sequence variants of this region over this specific region of amino acids have been described nor disclosed.

The skilled artisan cannot envision all the contemplated sequences based upon the general suggestion of a functional characteristic, translocation domain. The detailed chemical structure must be taught, therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Applicant's newly amended claim 1, seeks to change, modify, mutate, and alter the region of amino acids that the instant specification teaches are critical for attaining translocation domain activity for PE, but where or what changes will be tolerated, in light of the sequence combination of amino acids 280 to 344 defines a critical functional domain region of PE. Thus, the written description of the instant specification does not provide original descriptive support over the instantly claimed genus of molecules that share a highly variant domain II of PE, over a subfragment critical region of domain II, specifically amino acids 280 to 344 of SEQ ID NO 2.

Therefore, only those embodiments described and disclosed meet the written description requirement and not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page

1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

Conclusion

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on 7:30-5:00 M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
June 10, 2004

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